

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of

SUNG

Serial No. 09/990,874

Filed: November 21, 2001

For: XYLANASES WITH ENHANCED  
THERMOPHILICITY AND  
ALKALOPHILICITY

Group Art Unit: 1744

Examiner: Unassigned

Confirmation No. 2196

## SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

NEEDLE & ROSENBERG, P.C.  
Customer Number 23859

Sir:

Submitted herewith on Form PTO-1449 is a supplemental listing of documents known to applicants and/or their attorneys in compliance with the requirements of 37 C.F.R. § 1.56. A copy of each of these documents is enclosed.

The undersigned hereby certifies that each item of information contained in the Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing date of this Information Disclosure Statement.

Specifically, in accordance with the provisions of 37 C.F.R. § 1.97(e)(1), the information contained in this Supplemental Information Disclosure Statement was cited in a Partial

**ATTORNEY DOCKET NO. 07121.0003U1**  
**Application No. 09/990,874**

International Search Report of corresponding International Patent Application No. PCT/CA 01/01758 not more than three (3) months prior to the filing of this statement. A copy of the Partial Search Report, mailed November 25, 2003 is also enclosed.

Consideration of the cited documents and making the same of record in the prosecution of the above-noted application are respectfully requested.

No fee is believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

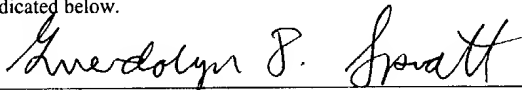


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**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8**

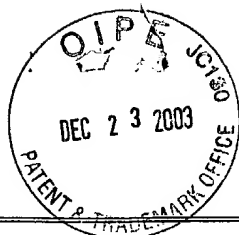
I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.



Gwendolyn D. Spratt

12-19-03

Date

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ATTORNEY DOCKET NO. 07121.0003U1

SERIAL NO. 09/990,874

CONFIRMATION NO. 2196

Page 1 of 2

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE (Rev. 7-80)  
PATENT AND TRADEMARK OFFICE

ATTORNEY DOCKET NO.: 07121.0003U1

SERIAL NO. 09/990,874  
CONFIRMATION NO. 2196LIST OF PRIOR ART CITED BY APPLICANT  
(Use several sheets if necessary)

APPLICANT: SUNG

FILING DATE: November 21, 2001

GROUP: 1744

## U.S. PATENT DOCUMENTS

EXAMINER INITIALS	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,866,526	2/02/99	Olsen et al.	51-	392	

## FOREIGN PATENT DOCUMENTS

	EP 0 828 002 A2	1997-05-09	Sung et al.			
	WO 00/29587	2000-05-25	Sun et al.			

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	Sapag et al. The endoxylanases from family 11: computer analysis of protein sequences reveals important structural and phylogenetic relationships" <i>J. Biotech.</i> 95:109-131, 2002

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

# PATENT COOPERATION TREATY

DEC 01 2003

**PCT GOWLING**

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
GOWLING LAFLEUR HENDERSON LLP  
Attn. Sechley, Konrad A.  
160 Elgin Street, Suite 2600  
Ottawa, Ontario K1P 1C3  
CANADA

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

**REGISTERED MAIL**

Applicant's or agent's file reference

08-893220WO

**PAYMENT DUE**

within 45 ~~xxxx~~ days  
from the above date of mailing

International application No.

PCT/CA 02/01758

International filing date  
(day/month/year)

20/11/2002

Applicant

NATIONAL RESEARCH COUNCIL OF CANADA

1. This International Searching Authority

- (i) considers that there are 6 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~ on the extra sheet:

- (ii) ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

see annex

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited**, within the time limit indicated above, to pay the amount indicated below:

EUR 945,00 x 5 = EUR 4.725,00  
Fee per additional invention      number of additional inventions      total amount of additional fees

Or, \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. see annex have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority



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NL-2280 HV Rijswijk  
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Authorized officer

Anna Sllberg

*AS*

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 2 47 48 50 61-66 (all partially),  
17-21 57-60 (all completely)

Modified xylanase comprising at least one substituted amino acid at position 11 but not a substituted amino acid at position 116, 118, 144 or 161 and does not comprise a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE), said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Xylanase comprising position 11, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16, an amino acid which is different from the amino acid found at position 11 in SEQ ID No. 16 as well as a xylanase comprising an acidic amino acid at position 11 and a non-polar amino acid at position 116 / or a non-aromatic hydrophobic amino acid at position 118, and a basic amino acid at position 144. Said modified xylanases characterized by a maximum effective temperature (MET) between 69 C (or 70 C) and 84 C, or a maximum effective pH (MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

2. Claims: 1 2 47-50 (all partially),  
26-29 51 52 (all completely)

Modified xylanase comprising at least one substituted amino acid at position 116 but not a substituted amino acid at position 11, 118, 144 or 161 and does not comprise a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE), said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Xylanase comprising at position 116, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16, an amino acid which is different from the amino acid found at position 116 in SEQ ID No. 16. Said modified xylanases characterized by a maximum effective temperature (MET) between 69 C (or 70 C) and 84 C, or a maximum effective pH

(MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

3. Claims: 1 2 47-50 61-66 (all partially),  
35-38 53 54 (all completely)

Modified xylanase comprising at least one substituted amino acid at position 118 but not a substituted amino acid at position 11, 116, 144 or 161 and does not comprise a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE), said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Xylanase comprising at position 118, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16, an amino acid which is different from the amino acid found at position 118 in SEQ ID No. 16. Said modified xylanases characterized by a maximum effective temperature (MET) between 69 C (or 70 C) and 84 C, or a maximum effective pH (MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

4. Claims: 1 2 47 48 50 61-66 (all partially), 3-6,  
55 56 (all completely)

Modified xylanase comprising at least one substituted amino acid at position 144 but not a substituted amino acid at position 11, 116, 118 or 161 and does not comprise a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE), said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Xylanase comprising at position 144, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16, an amino acid which is different from the amino acid found at position 144 in SEQ ID No. 16. Said modified xylanases characterized by a maximum effective temperature (MET)

between 69 C (or 70 C) and 84 C, or a maximum effective pH (MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

5. Claims: 1 2 47 48 50 61-66 (all partially),  
8-11 (all completely)

Modified xylanase comprising at least one substituted amino acid at position 161 but not a substituted amino acid at position 11, 116, 118 or 144 and does not comprise a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE), said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Xylanase comprising at position 161, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16, an amino acid which is different from the amino acid found at position 161 in SEQ ID No. 16. Said modified xylanases characterized by a maximum effective temperature (MET) between 69 C (or 70 C) and 84 C, or a maximum effective pH (MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

6. Claims: 1 2 47-49 61-66 (all partially) 7 12-16 21-25  
30-34 39-46 (all completely)

Modified xylanases comprising a Histidine at positions 10 and 105, a Methionine at position 27, a Leucine at position 29, an Alanine at positions 75 and 125, a Glutamic acid at position 129 (HML-AHAE) and at least one substituted amino acid at position 11, 116, 118, 144 and 161, said positions being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16. Said modified xylanases characterized by a maximum effective temperature (MET) between 69 C (or 70 C) and 84 C, or a maximum effective pH (MEP) between 5.8 and 8.4 (or 6 and 8), wherein modified xylanase is a Family 11 xylanase obtained from a *Trichoderma* species. Said modified xylanases characterized by a MET between 69 C and 84 C and a MEP between 5.8 and 7.6. Said

modified xylanases characterized by a MET between 70 C and 84 C and a MEP between 6.5 and 7.4. The use of said modified xylanase in an industrial process (pulp manufacturing).

The application as filed is considered to lack unity of invention since its subject-matter relates not to one but rather six separate inventions not linked together by a common underlying inventive concept as required by Rule 13.1 PCT.

According to Rule 13.2 PCT, an international patent application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features. Special technical features are such features that define the contribution of the claimed invention over the prior art.

The identified five inventions involve the technical feature of "substitution of at least the amino acid at position 11, 116, 118, 144 or 161 of a xylanase, said position being determined from sequence alignment with *Trichoderma reesei* xylanase II of SEQ ID No.16, said substitution being defined by the comparison to the wild type xylanase or to SEQ ID No.16". However, this feature cannot be accepted to constitute a special technical feature because it does not define a contribution over the prior art. Xylanases which such substitutions are well known in the art (see for example EP 0 828 002 A2; Turunen et al., Journal of Biotechnology 88 (2001), 37-46, cited by the applicant; US 5,866,529 to Olsen et al., 1999). The feature of "thermophilicity and/or alkalophilicity and/or expression efficiency" can also not be accepted as the special technical feature, since xylanases were already substituted to improve thermostability and alkalophilicity (EP 0 828 002 A2; Turunen et al., Journal of Biotechnology 88 (2001), 37-46, see page 38, left column, lines 27-33).

The contributions claimed in the present application which are allegedly made over the prior art correspond to the individual substitutions at positions 11, 116, 118, 144 and 161, respectively and to the combination of the so called HML-AHAE substitutions and at least one substitution at one of position 11, 116, 118, 144 or 161. These contributions are not so linked as to form one single inventive concept (Rule 13.1 PCT).

Searching these different subjects would have caused major additional searching efforts.

The application relates to a plurality of inventions, or groups of inventions, in the sense of Rule 13.1 PCT. They have been divided as defined above. If the applicant pays additional fees for one (or more) not yet searched group(s) of invention(s), then the further search(es) may reveal further prior art that gives evidence of a further lack of unity 'a posteriori' within one (or more) of the not yet searched group(s). In such a case only the first invention in this (each of these) group(s) of inventions, which is considered to lack unity of invention, will be the subject of a search.



No further invitation to pay further additional fees will be issued. This is because Article 17(3)(a) PCT stipulates that the ISA shall establish the International Search Report on those parts of the international application which relate to the invention first mentioned in the claims ('main invention') and for those parts which relate to inventions in respect of which the additional fees were paid. Neither the PCT nor the PCT guidelines provide a legal basis for further invitations to pay further additional search fees (W17/00, point 11 and W1/97, points 11-16).

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
- see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 828 002 A (CANADA NAT RES COUNCIL) 11 March 1998 (1998-03-11)	1,2, 17-20, 47,48, 50,57, 63,64 21
Y	table 2 examples 4,8 page 6, line 33 - line 38 ---	
X	TURUNEN OSSI ET AL: "A combination of weakly stabilizing mutations with a disulfide bridge in the alpha-helix region of Trichoderma reesei endo-1,4-beta-xylanase II increases the thermal stability through synergism." JOURNAL OF BIOTECHNOLOGY, vol. 88, no. 1, 2001, pages 37-46, XP002256879 ISSN: 0168-1656 cited in the application 1. Introduction 3.2 Thermostability 3.3 Temperature-dependent activity 3.5 Effect of pH on stability and activity table 1 figures 2-5 --- -/--	1,2, 17-20, 47,48,57

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 866 526 A (THELLERSEN MARIANNE ET AL) 2 February 1999 (1999-02-02)</p> <p>column 2, line 27 - line 33  column 2, line 52 - line 65  column 3, line 9 - line 18  column 3, line 58 -column 4, line 14  column 5, line 66 -column 6, line 12  column 7, line 12 - line 36  column 14, line 60 -column 15, line 3</p> <p align="center">---</p>	<p>1,2,47,  48,50,  57,59</p>
Y	<p>WO 00 29587 A (SUNG WING L ;IOGEN CORP (CA); TOLAN JEFFREY S (CA))  25 May 2000 (2000-05-25)  table 2</p> <p align="center">---</p>	<p>21</p>
P,X	<p>SAPAG AMALIA ET AL: "The endoxylanases from family 11: Computer analysis of protein sequences reveals important structural and phylogenetic relationships" JOURNAL OF BIOTECHNOLOGY, vol. 95, no. 2, 9 May 2002 (2002-05-09), pages 109-131, XP002256880  ISSN: 0168-1656  table 1  figure 1  in particular sequences 2, 12, 13, 21, 25, 36, 61-65, 73, 81 of Figure 1  cited for convenience to summarize the sequences known in the prior art</p> <p align="center">-----</p>	<p>50,57</p>

# Patent Family Annex

Information on patent family members

International Application No

PCT/CA 02/01758

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0828002	A	11-03-1998	US 5759840 A	02-06-1998
			CA 2210247 A1	09-03-1998
			DE 69712003 D1	23-05-2002
			EP 0828002 A2	11-03-1998
			JP 10179155 A	07-07-1998
			NZ 328680 A	27-04-1998
			US 5866408 A	02-02-1999
US 5866526	A	02-02-1999	AU 7807394 A	01-05-1995
			BR 9407752 A	04-03-1997
			CA 2173214 A1	13-04-1995
			CN 1134726 A	30-10-1996
			WO 9509909 A1	13-04-1995
			EP 0722491 A1	24-07-1996
			FI 961502 A	30-05-1996
			JP 9503130 T	31-03-1997
WO 0029587	A	25-05-2000	AU 1145100 A	05-06-2000
			CA 2385245 A1	25-05-2000
			WO 0029587 A1	25-05-2000
			EP 1131447 A1	12-09-2001

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Claims Nos.: 61-66 (all partially)

Present claims 61-66 relate to a modified xylanase obtained from a *Trichoderma* species defined by reference to desirable properties, namely a defined maximum effective temperature (MET) and/or a maximum effective pH.

The claims cover all xylanases from a *Trichoderma* species having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the xylanases obtained from a *Trichoderma* species comprising at least one substituted amino acid at position 11, 116, 118, 144 or 161, said position being determined from sequence alignment of said modified xylanase with *Trichoderma reesei* xylanase II amino sequence defined in SEQ ID No. 16.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.